in the homo-to-homo SCT group, hetero-to-homo SCT may be considered when immediate transplantation is required but an appropriate alternative donor is not available otherwise.

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HLA-C Mismatch without Impact on Outcome after Allogeneic HSCT

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In the present retrospective study we analyzed 382 patients undergoing HSCT between 1995 and 2011. Of these 115 patients received an HLA-C mm HSCT and 266 received an HLA-C matched graft. Only patients with malignant disease were included in the analysis with no significant differences between patients with HLA-C matched or mm donors. Median age was 42 (<1-68) versus 41 (<1-65) years in the matched and mm groups respectively. Early/late disease was 119/147 and 51/64, respectively (ns). Reduced intensity conditioning was given to 100 patients (38%) among HLA-C matched patients compared to 42 (37%) in the HLA-C mm group. Myeloablative conditioning was similar in both groups. Female donor to male recipient was given to 20 (8%) in the matched group versus 19 (17%) in the mm group. Bone marrow was used as stem cell source in 74 (28%) patients in the HLA-C matched group compared to 45 (39%) in the mm group (ns). The remaining patients received PBSC in each group. Median CD34 cell dose (x106/kg) was 7.2 (0.2-56.4) versus 7.1 (0.3-28.7), respectively. GVHD prophylaxis consisted of CsA + MTX in 84% versus 85% of the patients in each group. ATG was given to all patients before HSCT.

In the present material graft failure (GF) occurred in 9 (3.4%) in HLA-C matched group compared to 7 (6.1%) in the mm group (ns). In multivariate analysis for GF, major AB0 mismatch (p=0.03), RIC (p=0.01) and female donor to male recipient (p=0.002) were significant risk factors. HLA-C mm was not found to be significant (p=0.71). Neither had HLA-C mm any impact on mortality. Significant factors associated to mortality in multivariate analysis were: disease stage (p<0.001), year of HSCT (p=0.015) and donor age (p<0.001). For acute GVHD grades II-IV CsA+MTX (p<0.001) and RIC (p<0.001) decreased the risk whereas the use of PBSC (p=0.016) increased the risk. HLA-C matched patients compared to HLA-C mm showed no statistical difference regarding TRM, RFS, mortality, acute GVHD grades II-IV and relapse incidence. We also analyzed MFI for all HLA-C alleles which showed no significant correlation to outcome.

In conclusion, in the present study we find no negative impact of HLA-C mismatch on outcome after HSCT.

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Successful Engraftment and Full Donor Chimerism in Patients Undergoing Second Allogeneic Stem Cell Transplantation with Umbilical Cord Blood

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Background: Patients with graft failure or disease relapse following allogeneic hematopoietic cell transplant (HCT) have <10% survival with no intervention. Second HCT in this situation is becoming more common. Advantages of cord blood (UCB) in this setting include prompt availability of donor cells, no donor risk during cell procurement, and potential of enhancing the graft versus leukemia effect through use of highly mismatched grafts. We sought to determine the feasibility of second allogeneic transplant with UCB.
Methods: Twenty-three patients median age 33 yrs (range 4-69 yrs) received a CB transplant (CBT) as a second allogeneic HCT at the Fred Hutchinson Cancer Research Center between 2006–2013. Indication for second allograft were relapse (n = 19), graft failure (n = 3) and donor derived MDS (n = 1). Median time between transplants was 505 days (range, 55-3515). At the time of second HCT, 19 patients were in CR and 4 patients had persistent disease. For their second transplant, 10 patients received reduced intensity conditioning (RIC) with fludarabine (Flu) 200mg/m^2, cyclophosphamide (Cy) 50 mg/kg and 200-400 cGy TBI, 2 patients received myeloablative (MAC) conditioning with Flu 75mg/m^2, Cy 120mg/kg and 1200-1320cGy TBI (n = 2), and 11 patients received "midi" conditioning with treosulfan 42mg/kg, Flu 150-200mg/m^2 and 200 cGy TBI. All patients received GVHD prophylaxis with cyclosporine and mycophenolate mofeteil. Twenty of the 23 patients received a double CBT with a median TNC of 4.8 x 10^7 cells/kg and a median CD34+ of 2.2 x 10^5 cells/kg. Twelve patients received at least one 4/6 graft; 9 patients received at least one 5/6 graft.
Results: Median time to engraftment was 22 days (range day 6-49) among 21 evaluable patients; 2 patients died prior to engraftment. Median time to platelet engraftment was 55 days (range 23-83). Day +28 CD3+ chimerism was 100% second transplant donor in 16 of 19 evaluable patients, and 100% first donor in 2. One patient was mixed between first (22%) and second donor (78%). Death prior to Day 100 was seen in 5 patients (infection/organ failure (n = 3), encephalopathy (n = 1), and relapse (n = 1). Acute grade II-IV and III-IV GVHD was diagnosed in 18 of 21 and 6 of 21 evaluable patients respectively, and 9 of 16 evaluable patients developed chronic GVHD (6 mild, 2 moderate, 1 severe). Disease free survival, treatment related mortality, and relapse at 2 years was 40%, 33%, and 35% respectively. Patients receiving MAC/midi vs RIC conditioning experienced a 2-year DFS of 46 vs 15% (p = 0.02) and relapse rate of 26 vs 45% (p = 0.20).
Conclusions: Our results demonstrate quite favorable outcomes in patients undergoing CBT as a second allogeneic HCT, with all evaluable patients engrafting and full donor chimerism achieved in 16 of 19 patients by Day +28. The use of CB as the stem cell source is particularly attractive in this setting as it eliminates the need to put a conventional donor at risk.

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Low Incidence of Human Herpesvirus 6 Reactivation in Unmanipulated HLA-Haploidentical Related Stem Cell Transplantation with Corticosteroid As Graft-Versus-Host Disease Prophylaxis

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Human leukocyte antigen (HLA)-mismatced/haploidentical stem cell transplantation (SCT) is a known risk factor for human herpesvirus 6 (HHV-6) infection. High plasma HHV-6 DNA loads in peripheral blood have been associated with the development of HHV-6-associated encephalitis. However, previous results have been obtained in patients who underwent HLA-matched SCT or combined populations, including a small number of HLA-mismatched SCTs.